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TECH CENTER 1600/2900

Atty Dkt No. 0800-0024

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PATENT

AMENDMENT

In the Specification:

Please amend the specification as follows:

Please amend the paragraph beginning at page 17, line 3 as follows:

Serum, semen, urine, saliva, and stool samples were collected and subjected to PCR detection of AAV vector sequences. The 5' primer (5'-AGTCATCGCTATTACCATGG-3') (SEQ ID NO: 1) was derived from the CMV promoter and the 3' primer (5'-GATTTCAAAGTGGTAAGTCC-3') (SEQ ID NO: 2) was derived from intron I of human Factor IX. Amplified vector sequence yields a PCR fragment of 743 bp. For each sample, a control reaction containing the sample to be tested spiked with vector plasmid (50 copies/ $\mu$ g DNA) was also run to establish that the sample did not inhibit the PCR reaction. For semen, 3  $\mu$ g of DNA was analyzed (1  $\mu$ g in each of 3 separate reactions); for saliva, 1  $\mu$ g; and for urine, serum, and stool, DNA was extracted from 1-2 mL volume and analyzed. The sensitivity of the assay is 50 copies of vector sequence in 1  $\mu$ g DNA. Serum samples were positive for AAV vector sequences 24 and 48h post-injection and negative at time points thereafter. PCR reactions were performed in a total reaction volume of 100  $\mu$ L including 1.5 mM  $MgCl_2$  and 0.5  $\mu$ M of each primer. Following an initial denaturation step (94 °C for 4 min), 35 cycles of the following profile were carried out: Saliva samples were positive 24 h post-injection but negative thereafter. One patient had a positive urine sample 24 h post-injection but was negative thereafter. All other samples were negative for AAV vector sequences, including serum samples taken up to 59 days after AAV vector injection.